



NDA 19-962/S-022

AstraZeneca  
Attention: Ms. Cindy M. Lancaster  
1800 Concord Pike  
P.O. Box 8355  
Wilmington, DE 19803-8355

Dear Ms. Lancaster:

Please refer to your supplemental new drug application dated July 6, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Toprol XL (metoprolol succinate) 25, 50, 100 and 200 mg Tablets.

We acknowledge receipt of your submissions dated December 14, 2001.

This "Changes Being Effected" supplemental new drug application provides for final printed labeling revised as follows:

1. The third paragraph of the CLINICAL PHARMACOLOGY/Clinical Trials subsection has been changed from:

However, in the US subgroup and women, overall mortality and cardiovascular mortality appeared less affected.

To:

However, in the US subgroup (n=1071) and women (n=898), overall mortality and cardiovascular mortality appeared less affected.

2. The following subsection has been added to the ADVERSE REACTIONS section of the labeling:

**Post-Marketing Experience**

The following adverse reactions have been reported in post-marketing use:

**GASTROINTESTINAL:** hepatitis.

**MUSCULOSKELETAL:** arthralgia.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the final printed labeling included in your July 6, 2001 submission. Accordingly, the supplemental application is approved effective on the date of this letter.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2  
FDA  
5600 Fishers Lane  
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call Ms. Zelda McDonald, Regulatory Health Project Manager, at (301) 594-5333.

Sincerely,

*{See appended electronic signature page}*

Douglas Throckmorton, M.D.  
Acting Director  
Division of Cardio-Renal Drug Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

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/s/

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Doug Throckmorton  
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